

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1-2. (Cancelled)

3. (Currently amended) A method of increasing muscle function in a subject suffering from wasting, said method comprising administering to said subject a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B) (SEQ ID NO: 1)

wherein,

A1 is Tyr or His;
A2 is Val or Ala;
A8 is Asn or Ser;
A13 is Val or Ile;
A15 is Ala or Gly;
A18 is Ser or Tyr;
A24 is Gln or His;

A25 is Asp or Glu;

A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of 1 up to 15 residues; and

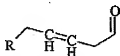
R0 is NH_2 or $\text{NH}-(\text{CH}_2)_n-\text{CONH}_2$, with $n=1$ to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

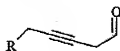
wherein the backbone can be substituted by C_{1-6} alkyl, C_{3-6} cycloalkyl, or C_{6-12} aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C_{3-9} cycloalkyl, and C_{6-12} aryl.

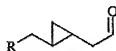
4. (Original) The method of claim 3, wherein X is selected from the group consisting of:



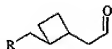
- 1 (R=H or CH₃ or CH₂CH₃)
cis or *trans*



- 2 (R=H or CH₃ or CH₂CH₃)



- 3 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



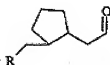
4 ($\text{R}=\text{H}$ or CH_3 or CH_2CH_3)

cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



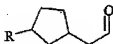
5 ($\text{R}=\text{H}$ or CH_3 or CH_2CH_3)

cis or *trans*, (when $\text{R} \neq \text{H}$)



6 ($\text{R}=\text{H}$ or CH_3 or CH_2CH_3)

cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



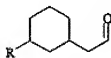
7 ($\text{R}=\text{H}$ or CH_3 or CH_2CH_3)

cis or *trans*, (when $\text{R} \neq \text{H}$)
both as racemic mixtures
or pure enantiomeric pairs

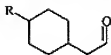


8 ($\text{R}=\text{H}$ or CH_3 or CH_2CH_3)

cis or *trans*, both as racemic mixtures
or pure enantiomeric pairs



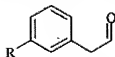
- 9 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)
 both as racemic mixtures
 or pure enantiomeric pairs



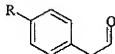
- 10 (R=H or CH₃ or CH₂CH₃)
cis or *trans*, (when R \neq H)



- 11 (R=H or CH₃ or CH₂CH₃)

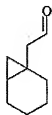


- 12 (R=H or CH₃ or CH₂CH₃)



- 13 (R=H or CH₃ or CH₂CH₃)

and



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5. (Original) The method of claim 3, wherein A30 is selected from the group consisting of:
- (a) a bond;
 - (b) an amino acid sequence corresponding to positions 30-44 of a natural GRF peptide, and
 - (c) said amino acid sequence of (b) having a 1-14 amino acid deletion from its C-terminus.
6. (Original) The method of claim 3, wherein said GRF peptide is selected from the group consisting of:
- (a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3;
 - (b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5; and
 - (c) said polypeptide of (a) having a 1 to 14 amino acid deletion from its C-terminus.
7. (Previously presented) The method of claim 3, wherein said GRF analog is (hexenoyl trans-3)hGRF(1-44)NH₂ (SEQ ID NO: 7).
8. (Previously presented) The method of claim 3, wherein said muscle function is selected from the group consisting of:
- (a) muscle strength;
 - (b) muscle endurance; and
 - (c) both (a) and (b).

9. (Original) The method of claim 8, wherein said muscle function is muscle strength.
10. (Original) The method of claim 9, wherein said muscle strength is peripheral muscle strength.
11. (Original) The method of claim 8, wherein said muscle function is muscle endurance.
12. (Previously presented) The method of claim 3, wherein said increase results in a reduction of a parameter selected from the group consisting of:
 - (a) breathing discomfort;
 - (b) leg discomfort; and
 - (c) both (a) and (b).
13. (Previously presented) The method of claim 3, wherein said increase results in an increase in lean body mass in said subject.
14. (Previously presented) The method of claim 3, wherein said increase results in a decrease in fat mass in said subject.
15. (Cancelled)
16. (Currently amended) The method of claim 3-15, wherein said wasting is associated with a condition selected from the group consisting of chronic obstructive pulmonary disease, chronic renal failure, congestive heart failure, human immunodeficiency virus infection, acquired immunodeficiency syndrome, cancer, malnutrition, frailty, immobilization paraplegia and spinal disorder.
17. (Previously presented) The method of claim 3, wherein said subject suffers from severe wasting.

18. (Original) The method of claim 17, wherein said subject has a body mass index less than or equal to 20.
19. (Original) The method of claim 17, wherein said subject has a weight less than 90% of ideal body weight.
20. (Original) The method of claim 17, wherein said subject is a male and said subject has a fat free mass index less than or equal to 16.
21. (Original) The method of claim 17, wherein said subject is a female and said subject has a fat free mass index less than or equal to 15.
22. (Previously presented) The method of claim 3, wherein said GRF analog is administered through a route selected from the group consisting of intravenous, oral, transdermal, subcutaneous, mucosal, intramuscular, intranasal, intrapulmonary, parenteral, intrarectal and topical.
23. (Previously presented) The method of claim 3, wherein said GRF analog is administered in a dose from about 0.0001 mg to about 4 mg.
24. (Previously presented) The method of claim 23, wherein said GRF analog is administered in a dose selected from the group consisting of about 1 mg and about 2 mg.
- 25-80. (Cancelled)